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**REMARKS**

This Reply is responsive to the Office Action mailed November 29, 2004 (hereinafter the "present Office Action"). Claims 11 and 12 are pending. Claims 2-10 and 13-28 were previously canceled without waiver or prejudice to their presentation in a later filed action claiming the benefit of priority of the present application.

Claim 11 has been amended to better distinguish the present polyester over the prior art by replacing "absorbable" with "biodegradable". Support for this amendment is found in the specification at page 5, lines 19 - 22. Claim 1 has also been amended to correct a typographic error by replacing "ε-caproic acid" with "ε-hydroxy caproic acid". Support for this amendment may be found throughout the application particularly at page 7, lines 7-9.

Reconsideration of the present Office Action and allowance of the application, as amended, are respectfully requested.

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1. Applicants are grateful for the withdrawal of the finality of the previous Office Action pursuant to the Request for Continued Examination under 37 C.F.R. 1.114 submitted August 20, 2004.

2. Applicants are grateful for the withdrawal of the rejections of claims 11 and 12 under 35 U.S.C. §112(2).

3. Claim 11 has been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 4,487,860 issued to Winner et al. (hereinafter referred to as "Winner") in view of U.S. Patent No. 2,729,609 issued to Tess et al. (hereinafter referred to as "Tess"). In particular, the Examiner reasons that "[i]t would have been obvious to one of ordinary skill in the art to modify the phosphated polyester of Winner et al. by adding lactic acid as a monomer component therein because (1) Winner et al. teaches phosphated polyesters, in general; (2) Winner et al. and Tess are both drawn to compositions for coating surfaces; (3) Winner et al. and Tess et al. comprise similar components (i.e. dicarboxylic acids, polyols, and monocarboxylic acids); and (4) Tess et al. teaches that lactic acid is useful in such surface coating polymer compositions...[an as such]...[o]ne would have been motivated to utilize the lactic acid as a monomer in the compositions of Winner et al. because, as taught by Tess et al., such modifying agents are useful in preparing non-drying alkyds."

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Applicants respectfully submit that the Examiner has not met his initial burden to establish a *prima facie* case of obviousness as mandated by *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1990). See MPEP §§2143 - 2143.03.

With respect to the first criteria, the Examiner has failed to provide some suggestion of the desirability of doing what the Inventors of this application have done. "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or implicitly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the

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references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). See MPEP §§2144 - 2144.9. The Examiner fails to provide an expressed or implicit suggestion to combine the teachings of Winner with that of Tess. When the motivation to combine the teachings of the references is not immediately apparent, it is the duty of the examiner to explain why the combination of the teachings is proper. *Ex parte Skinner*, 2 USPQ2d 1788 (Bd. Pat. App. & Inter. 1986). See MPEP §2142. Applicants contend that, based on the following observations, the aforementioned line of reasoning presented by the Examiner in support of the combination of Winner and Tess, is flawed and as such, fails to meet the requirements of *Skinner*.

Applicants respectfully submit that since both the Winner and Tess references are not analogous prior art, the Examiner's observation that both are directed to the same subject matter, i.e., the 2<sup>nd</sup> point in support of the combination, is fatally flawed<sup>1</sup>. "A reference is reasonably pertinent if ... it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem." *Wang Laboratories, Inc. v. Toshiba Corp.*, 993 F.2d 858, 26 USPQ2d 1767 (Fed. Cir. 1993) and *State Contracting Engineering Corp. v. Condotte America, Inc.*, 346 F.3d 1057, 1069, 68 USPQ2d 1481, 1490 (Fed. Cir. 2003). See, MPEP §2141.01(a).

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The present invention is directed to novel carboxyl-bearing absorbable polyesters for use in forming conjugates with bioactive polypeptides as controlled release systems (See page 1, lines 29 - 31 of the instant application). Winner, on the other hand, is directed to "aqueous blends containing certain reactive self-curing water-dispersed polymers, certain water dispersed polyelectrolyte polymers, and preferably containing a polymeric phosphate additive," (See, Winner col. 1, lines 11 - 14) which is capable of forming a "relatively rigid or hard polymer particle surface" (See, Winner col. 1, lines 51 - 52) which is "particularly suitable for beverage cans" (See, Winner col. 1, lines 63 - 64). The Winner blend preferably contains phosphated polymers which provide "improved coating characteristics such as solvent resistance and improved porosity properties" (See, Winner, col. 2, lines 1 - 2). Tess is directed to a resin comprised of "a mixture [of] ... a polybasic acid or derivative thereof, a polyhydric alcohol and a modifying agent containing a poly-tert-alkyl-substituted carboxylic monocarboxylic acid, such as 3,5-di-tert-butyl-benzoic acid and... an additional modifying agent" (See Tess, col. 1, lines 22 - 27)... which is useful as a "surface coating.. and particularly lacquers and baking enamels." The Applicants submit that the resins and blends of Winner and Tess used to coat cans and baking equipment would not "have commended ...

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<sup>1</sup> Applicants assume that the Examiner is of the opinion that the subject matter of the instant application,

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an inventor's attention" relevant to a polymer used for the controlled release of a bioactive agent in a pharmaceutical, and as such both reference are not analogous to the teachings of the instant application<sup>2</sup> and as such, the Examiner's 2<sup>nd</sup> point in his reasoning for combining Winner and Tess, i.e., that Winner and Tess are drawn to the same subject matter, is flawed.

As a digression, the Applicants contend that the phosphorous-containing heterochain polymers disclosed by Winner and Tess are similar to those discussed at page 1, lines 13 - 24 of the instant application. As stated by the Applicants, at the time the instant application was filed, "conditions of chemical reactions known for hydroxyl group phosphorylation could cause hydrolysis of the highly reactive absorbable polyester chains." See, page 1, lines 24 - 29. Applicants contend that since there was no reasonable likelihood of success that polymers similar to those of Winner and Tess would be suitable for use in sustained-release pharmaceutical compositions, the 2<sup>nd</sup> prong of *In re Vaeck* has not been met.

With respect to the 3<sup>rd</sup> prong of the requirements of *In re Vaeck*, requiring that the prior art references, when combined, must teach or suggest all of the claim limitations, Applicants respectfully submit that the cited

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and that of Winner and Tess are the same for the Examiner's line of reasoning to be valid.

<sup>2</sup> The Examiner's several references to "coating surfaces" leads the Applicants to believe that the Examiner may not appreciate the subject matter of the instant application.

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references fail to do so. Claim 11 is directed to the following:

A ① biodegradable polyester with ② at least one monophosphate functionality per absorbable polyester chain wherein said monophosphate functionality comprises a ③  $-O-P(O)(OH)_2$  moiety ④ covalently linked to said polyester chain via ⑤ a single phosphate bond, and wherein the polyester chain consists essentially of ⑥ one or more monomers selected from the group consisting of L-lactic acid, D-lactic acid, DL-lactic acid, malic acid, citric acid, tartaric acid,  $\epsilon$ -hydroxy caproic acid, alkylene oxalate, cycloalkylene oxalate, alkylene succinate,  $\beta$ -hydroxybutyrate, glycolide, glycolic acid, L-lactide, D-lactide, DL-lactide, meso-lactide, trimethylene carbonate,  $p$ -dioxanone, 1,5-dioxepan-2-one and 1,4-dioxepan-2-one and any optically active isomers, racemates, or copolymers thereof.

As indicated above, claim 11 has six limitations that all must be found in the prior art cited against the instant application. "To establish a prima facie case of obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). See MPEP §2143.03. Applicants respectfully contend that Winner, in combination with Tess, does not teach or suggest the six limitations recited above.

With respect to Winner, the primary reference cited against the patentability of the instant application, as stated previously, the *blends* of Winner are designed

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"provide a relatively rigid or hard polymer particle surface." See, Winner col. 1, lines 51 - 52. The phosphorylated polymer is included in the blend to improve the solvent resistance and porosity of the polymer coating. As such, the phosphorylated polymers of Winner do not "undergo chain dissociation in a biological environment to water soluble by products as a function of time, See, instant application at page 5, lines 19 - 22, and are thus ① "biodegradable," as do the claimed polyesters of the instant application.

There is also no disclosure anywhere in Winner that the polyesters described therein have ② at least one monophosphate functionality per polyester chain as required by claim 11. To the contrary, there is a suggestion in Winner that not every chain is phosphorylated. See, Winner col. 7, lines 48 - 51.

As stated in the instant application at page 5, lines 27 - 30, the Inventors selected the particular monophosphate moiety, i.e., ③  $-O-P(O)(OH)_2$  moiety, so that "two additional acid -OH groups [would] be available for conjugation or neutralization." See, page 5, lines 28 - 29. Winner does not recognize the benefits of the free -OH as implicitly required by claim 11. To create the free -OH groups, the phosphate moiety of the instant application is "④ covalently bonded to the polyester chain" via "⑤ a single phosphate bond". Winner does not require use of a



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single phosphate bond and suggests that the phosphate is ionically bonded to the polyester. See, Winner col. 7, lines 61 - col. 8. line 5.

As acknowledged by the Examiner, Winner does not disclose any of the monomers of claim 11.

Tess makes no reference to a ① biodegradable polyester with ② at least one monophosphate functionality per chain having a ③  $-O-P(O)(OH)_2$  moiety ④ covalently linked via ⑤ a single phosphate bond wherein the polyester chain consists of, i.e., "must have," ⑥ one or more monomers selected from the group consisting of L-lactic acid, D-lactic acid, DL-lactic acid<sup>3</sup>, malic acid, citric acid, tartaric acid,  $\epsilon$ -hydroxy caproic acid, alkylene oxalate, cycloalkylene oxalate, alkylene succinate,  $\beta$ -hydroxybutyrate, glycolide, glycolic acid, L-lactide, D-lactide, DL-lactide, meso-lactide, trimethylene carbonate, p-dioxanone, 1,5-dioxepan-2-one and 1,4-dioxepan-2-one and any optically active isomers, racemates, or copolymers thereof. As such, Tess does not supply the limitations missing from the primary reference, and as such, the combination cited by the Examiner, i.e., Winner in view of Tess, in support of the rejection of claim 11 under 35 U.S.C. 103(a), does not meet the requirement of *In re Royka*.

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<sup>3</sup> Although Tess refers to lactic acid as a possible modifying agent, it does not require use thereof. It should be noted that of the other monomer sources identified in claim 11, no other are identified in Tess.

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Applicants respectfully request the reconsideration of the rejection of claim 11 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 4,487,860 issued to Winner et al. in view of U.S. Patent No. 2,729,609 issued to Tess et al. Applicants contend that based on the above-argument that said rejection is erroneous and/or has been overcome by amendment. Applicants respectfully request the withdrawal of said rejection.

The Examiner's comments with respect to the recitation of the "absorbable" nature of the claimed peptides have been overcome by the above amendment of claim 11.

Claim 12 has been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 4,487,860 issued to Winner et al. in view of U.S. Patent No. 2,729,609 issued to Tess et al. and in further view of U.S. Patent No. 5,686,540 issued to Kakizawa (hereinafter referred to as "Kakizawa"). Applicants assert that since claim 11, upon which claim 12 is dependent thereon, is nonobvious over Winner and Tess, claim 12 is also nonobvious over Winner and Tess, either alone or in combination. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Although Kakizawa may teach a polyethylene glycol as a component of the phosphorylated polyesters, it does not supply missing limitations, ①, ②, ③, ④, ⑤ or ⑥, as noted above. As such, Kakizawa, either alone or in combination with Winner and/or Tess does not teach each and every limitation found in claim 12, and as

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such, does not render claim 12 obvious. Applicants respectfully request the reconsideration and withdrawal of the rejection of claim 12 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 4,487,860 in view of U.S. Patent No. 2,729,609 and in further view of U.S. Patent No. 5,686,540.

4. Applicants respectfully request entry of the amendment replacing "ε-caproic acid" with "ε-hydroxy caproic acid". Applicants submit that one skilled in the art would recognize that does not exist. As is known by the skilled artisan, the Greek letter "ε-" is placed before a substituent of a chemical entity, such as caproic acid, to indicate the position of the substituent. As written, ε-caproic acid fails to identify the substituent. As stated at page 7, lines 7-9 of the instant application, the Applicants state that "the present invention is directed to monophosphate analogues of several types of *hydroxylic* oligomers and polymers." Applicants contend that one skilled in the art would recognize that the reference to "hydroxyl" was inadvertently omitted from "ε-caproic acid" and that the Applicants intended "ε-hydroxy caproic acid".

#### **CONCLUSION**

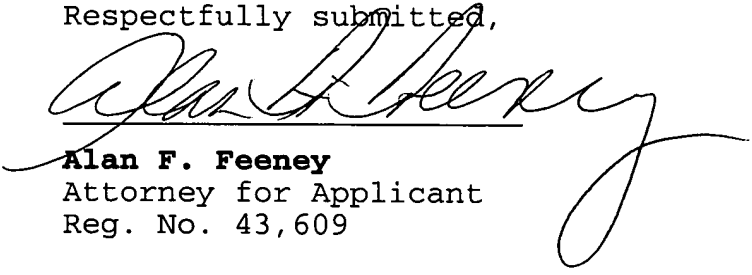
Based on the above remarks, Applicants submit that all of the rejections and objections have been overcome and that all pending claims are now in a condition for allowance,

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which action is respectfully requested. Should Examiner Mitchell deem that any further action by the Applicants would put this application in order for acceptance, he is requested to contact the Applicants' undersigned representative.

The Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. 50-0590.

Respectfully submitted,  
Date: 5/31/2005

  
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